Topics in Primary Care Medicine

Prostatitis: Still a Diagnostic and Therapeutic Dilemma

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"Topics in Primary Care Medicine" presents articles on common diagnostic or therapeutic problems encountered in primary care practice. Physicians interested in contributing to the series are encouraged to contact the series' editors.

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"Prostatitis" is a diagnosis frequently made by primary care physicians and urologists on the basis of symptoms noted by patients and a few clinical findings. However, it is sometimes unclear whether physicians who use this diagnosis are referring to the same entities. If prostatitis is defined as inflammation of the prostate gland as determined by increased numbers of leukocytes in the prostatic fluid, it has been reported that as many as 20% of new patients presenting to a urology clinic have evidence of prostatic inflammation. On the other hand, the variety of other symptoms, signs and findings purported to characterize prostatitis are diverse and poorly understood. Too often prostatitis is diagnosed in any patient who presents with complaints of voiding and ejaculatory disturbances, perineal aching, low back pain and prostatic tenderness to palpation.

To clarify discussion of this problem, prostatitis can be divided into three categories: *acute and chronic bacterial prostatitis, nonbacterial prostatitis* and *prostatodynia.* Those patients with bacterial prostatitis have documented bacterial infections of the prostate. Those with nonbacterial prostatitis have evidence of prostatic inflammation, but no sign of bacterial infection. Those with prostatodynia have complaints associated with prostatitis without bacterial infection or inflammation.

Although few laboratory tests are available to support a diagnosis of prostatitis, two tests are useful in classifying patients who present with symptoms of prostatitis into the correct category. First, patients can be grouped into those who have or do not have bacterial infection of the prostate. True bacterial infections of the prostate are either acute or chronic, and most commonly involve the Gram-negative organisms *Escherichia coli* and *Enterobacter, Serratia, Klebsiella* and *Pseudomonas* species. Collection of segmented urine specimens, as originally described by Meares and Stamey, is the accepted way of diagnosing bacterial prostatitis. To collect these specimens in an uncircumcised patient the foreskin is taped back and the meatus is cleansed with soap and dried; in a circumcised patient no special preparation is needed. When the patient states that he has a very full bladder, he is asked to void and the examiner collects four specimens for quantitative bacterial cultures: (1) the first 5 to 10 ml voided (VB_1 "the voided bladder-1") to show urethral organisms; (2) a midstream specimen (VB_2, "voided bladder-2") to show bladder organisms; (3) prostatic fluid (EPS, "expressed prostatic secretions"), obtained by prostatic massage for culture and microscopic examination, to show prostatic organisms; and (4) the first 5 to 10 ml voided after prostatic massage (VB_3, "voided bladder-3") to show a combination of urethral and prostatic organisms.

Bacterial infection is localized to the prostate if the number of bacterial colonies cultured from the EPS or VB_3 is at least ten times greater than that found in the urethral VB_1 specimen. The bladder urine (VB_2) should be sterile at the time of localization. Isolated examination and culture of prostatic fluid alone (or even cultures of prostatic fluid and bladder urine) cannot be used to diagnose bacterial prostatitis because urethral organisms may contaminate the prostatic fluid specimen during collection and cause misleading results.

The second test, microscopic examination of the

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ABBREVIATIONS USED IN TEXT

VB_1 = voided bladder-1 (the first 5 to 10 ml of voided urine)
VB_2 = voided bladder-2 (a midstream specimen)
EPS = expressed prostatic secretions
VB_3 = voided bladder-3 (the first 5 to 10 ml of urine voided after prostatic massage)

prostatic fluid, will define patients with prostatic inflammation. In patients with nonbacterial prostatitis and acute and chronic bacterial prostatitis, prostatic inflammation usually is shown by the presence of more than 15 leukocytes and occasional oval fat macrophages per high-powered microscopic field (400 to 450 times magnification) of prostatic fluid. Patients with prostatodynia do not have abnormal numbers of leukocytes in their prostatic fluid.

Acute Bacterial Prostatitis

Patients with acute bacterial prostatitis usually complain of a sudden onset of malaise, low back and perineal pain, chills, fever and obstructive and irritative voiding symptoms, such as dysuria, urinary frequency and intermittent urine stream. On prostatic examination there may be a nodular or normal-feeling gland that is painful to palpation. A Gram-negative bacterial pathogen can usually be cultured from the prostatic fluid, but because of prostatic pain and the risk of massage disseminating bacteria from an acutely infected prostate into the systemic circulation, one should probably not perform prostatic massage during the acute illness. Moreover, since bacteriuria is usually present during acute prostatitis, the bacterial pathogen can be cultured from the voided urine specimen, and results of prostatic fluid cultures (EPS) are uninterpretable when the bladder urine is infected.

These patients are often acutely ill and may need to be admitted to hospital for treatment with parenteral antimicrobials, such as aminoglycosides and ampicillin. Once cultures and sensitivities are obtained, treatment with an orally given antimicrobial agent to which the organism is sensitive (such as trimethoprim-sulfamethoxazole, 160 mg/800 mg twice a day) should be continued at full dosage for three to four weeks to prevent the development of chronic bacterial prostatitis. The severe prostatic inflammation in acute bacterial prostatitis allows many antimicrobial agents that would ordinarily be excluded from the prostate gland to enter in concentrations sufficient to cure the infection. In fact, perhaps as a result of this property, acute bacterial prostatitis is probably the most successfully treated of the prostatitis syndromes.

Any bladder outlet obstructive symptoms caused by the inflammation and swelling of the infected prostate are probably best treated with a temporary percutaneous suprapubic drainage catheter. This will prevent further irritation of the prostate that a urethral catheter may cause.

Chronic Bacterial Prostatitis

Patients with chronic bacterial prostatitis present with a variety of symptoms. In some patients intermittent bladder irritative symptoms develop and chronic perineal aching or low back pain occurs, while others are almost asymptomatic even when bacteriuric. Prostatic examination usually reveals a gland which is normal to palpation. The most common characteristic of these patients is a history of recurring urinary infections caused by the same organism. Since the prostate acts as a nidus for these infections, routine antimicrobial therapy clears the bladder infection only temporarily until the prostatic bacteria reinfect the bladder. Patients who present with bacteriuria must be cleared of their bladder infection before lower tract segmented urine cultures can be done to localize the infection to the prostate. This may be done by initiating therapy with antimicrobial agents, such as nitrofurantoin, tetracycline or nalidixic acid, which do not enter the prostatic fluid in significant concentrations. After the patient has taken the drug for several days, segmented urine cultures are collected. To accurately diagnose chronic bacterial prostatitis, these cultures must demonstrate bacterial infection of the prostate, and microscopic examination of the prostatic fluid should show increased numbers of leukocytes and macrophages. Since segmented urine cultures sometimes may be difficult or inconvenient to obtain, especially following transurethral resection of the prostate, long-term antimicrobial therapy may be indicated for suspected bacterial prostatitis if a male patient has had documented recurrent bacteriuria with the same organism and no other source of bacterial persistence can be identified.

The therapy for chronic bacterial prostatitis is often frustrating. Few antimicrobial agents have been shown to diffuse into the prostate and prostatic fluid in concentrations adequate for treatment and cure of the common Gram-negative organisms responsible for infection. Two orally given drugs that may reach therapeutic levels are trimethoprim-sulfamethoxazole (160 mg/800 mg twice a day) and carbenicillin indanyl sodium (764 mg four times a day). When started, administration of these drugs should be continued for at least a month and possibly as long as three months. However, clinical studies have shown that only about 50% of patients with chronic bacterial prostatitis who are treated for 90 days with full-dose trimethoprim-sulfamethoxazole are cured. Although this high therapeutic failure is sometimes due to infected prostatic calculi, it is probably more frequently due to bacterial persistence in prostatic foci that fail to be reached by antimicrobial agents. In those patients in whom treatment fails, daily low-dose antimicrobial therapy with a drug to which the organism is sensitive (such as nitrofurantoin, 50 or 100 mg a day, or trimethoprim-sulfamethoxazole, 40 mg/200 mg a day, half a regular tablet) will prevent relapsing bladder infections and render the patient asymptomatic by sterilizing the urine daily and thereby suppressing bacteriuria.

Although zinc levels from the prostatic fluid of pa-

tients with bacterial prostatitis are lower than those from normal men, there is no convincing evidence that oral zinc administration increases prostatic fluid zinc or that zinc supplementation decreases bacterial or nonbacterial prostatitis. Transurethral resection of the prostate is curative in fewer than 50% of patients with bacterial infection. This is probably because the bacteria tend to be located in areas of the prostate that are not routinely removed in this operation. Thus the side effects of transurethral resection of the prostate, such as retrograde ejaculation, and the suboptimal success rate may render this therapeutic option unacceptable to many patients with bacterial prostatitis; however, these patients are best referred to a urologist for consideration of different modalities of treatment.

Nonbacterial Prostatitis

Patients with nonbacterial prostatitis may present with complaints indistinguishable from those of chronic bacterial prostatitis but without documented episodes of bacterial cystitis. Often they complain of perineal discomfort, and prostatic examination reveals a normal prostate. Although some studies have implicated mycoplasma and chlamydiae as causes of nonbacterial prostatitis, these agents have not yet been proved to be responsible for most cases. Microscopic examination of the prostatic fluid shows inflammation with increased numbers of leukocytes, but segmented urine cultures reveal no prostatic foci of Enterobacteriaceae. It has been reported that in 75% to 80% of men with prostatic inflammation no infectious agent can be found.

Because the source of inflammation in this disease is unknown, therapy is usually unsatisfactory. Because chlamydia and mycoplasma are difficult to culture and are not even sought by most bacteriology laboratories, a therapeutic trial with tetracycline (500 mg four times a day) or doxycycline (100 mg twice a day for two to three weeks) or erythromycin (500 mg four times a day for two to three weeks) is reasonable. However, if no improvement occurs, use of an anti-inflammatory agent like indomethacin or ibuprofen will sometimes give symptomatic relief. Finally, the patient should be counseled that he does have inflammation of his prostate, but it is not related to known infections, cancer or venereal disease.

Prostatodynia

Patients with prostatodynia suffer from a variety of perineal, ejaculatory and voiding complaints that are similar to those observed in patients with chronic bacterial or nonbacterial prostatitis. Examination shows a normal prostate; segmented urine cultures for prostatic localization show no evidence of prostatic bacteria, and these patients, as is true for those with nonbacterial prostatitis, give no documented history of bacteriuria. However, these patients differ from those with nonbacterial prostatitis because microscopic examination of the prostatic fluid shows no evidence of inflammation; hence, this is not a true "prostatitis." The cause of the symptoms in these patients is not understood. Studies have shown that psychologic disturbance, pelvic and perineal muscle spasm, and abnormal spasm of the urethral sphincter during voiding may contribute to a patient's symptoms.

Because there probably are multiple causes for the findings in prostatodynia, no single therapy is effective. Most treatments for the other prostatic syndromes are unsuccessful when applied to patients with prostatodynia because neither inflammation nor infection is present. For those patients who are thought to suffer from abnormal sphincter spasm during voiding, a trial with an α-adrenergic blocking agent such as phenoxybenzamine hydrochloride, 10 mg at bedtime or twice a day, or a muscle relaxant such as diazepam, may produce symptomatic relief. Patients with persistent complaints of frequency, voiding discomfort and suprapubic pain may need to be evaluated for the presence of a bladder tumor, carcinoma in situ or interstitial cystitis. If these abnormalities are absent, the patient should be reassured that no serious disorder has been discovered and that his symptoms are unrelated to venereal disease or cancer. Furthermore, he should be told that his symptoms may intermittently disappear and reappear.

Summary

Although diagnosis of the prostatitis syndromes is often cumbersome and therapy sometimes disappointing, classification of these syndromes allows a more rational therapeutic approach toward treatment of these patients. By carefully selecting patients who have bacterial infection of the prostate, the physician may identify those who may respond to a course of antimicrobial agents. However, because in most of those with nonbacterial prostatitis and prostatodynia there will be no response to antimicrobials, the administration of multiple long courses of such agents can be avoided. Likewise, use of anti-inflammatory agents in patients with prostatodynia can be avoided, and other approaches such as α-blockers or even psychotherapy may be tried.

Though some patients with bacterial prostatitis or nonbacterial prostatitis, and even an occasional patient with prostatodynia, may be cured with present means, the optimal curative treatment remains unknown. Future work defining the causes of nonbacterial prostatitis and prostatodynia may provide new approaches to their management.

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